REMARKS

Claims 1-8 are pending in the application. Applicant thanks the Examiner for allowing claims 4 and 5. In the present Amendment, claim 1 is amended to incorporate the limitations of claim 2, and claim 6 is amended to incorporate the limitations of claim 7. Claims 3 and 8 are amended to delete reference to claims 2 and 7, respectively. Claims 2 and 7 are canceled without prejudice. Upon entry of the above-made amendments, claims 1, 3-6 an 8 will be pending in the application. Applicant reserves the right to prosecute the subject matter of any canceled claims, or any unclaimed subject matter, in a related application.

No new matter has been added by these amendments. Entry of the foregoing amendments and consideration of the following remarks are respectfully requested.

The Rejection Under 35 U.S.C. § 112, First Paragraph, For Lack of Enablement, Should Be Withdrawn

The Examiner has rejected claims 6-8 under 35 U.S.C. § 112, first paragraph, as allegedly nonenabled. Applicant has amended claim 6 and canceled claim 7; thus, Applicant traverses as follows with respect to claims 6 and 8.

Analysis of enablement requires a determination of whether the "disclosure, when filed, contained sufficient information regarding the subject matter of the claims as to enable one skilled in the pertinent art to make and use the claimed invention." MPEP 2164.01 at page 2100-178. One skilled in the art is presumed to use the information available to him in attempting to make or use the claimed invention. *See Northern Telecom, Inc. v. Datapoint Corp.*, 908 F.2d 931, 941 (Fed. Cir. 1990). The standard for determining whether a claim is enabled or not is whether it requires undue experimentation to practice. *Id.*; *see also Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916); *In re Wands*, 858 F.2d 731, 737, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988). In *Wands*, the Federal Circuit outlined several non-exclusive factors to consider in a determination of whether claims were enabled, including: A) the breadth of the claims; (B) the nature of the invention; (C) the state of the prior art; (D) the level of one of ordinary skill; (E) the level of predictability in the art; (F) the amount of direction provided by the inventor; (G) the existence of working examples; and (H) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In *Wands*, the Federal Circuit held that a particular method requiring substantial experimentation was nonetheless enabled, because the experimentation was routine.

Applicant traverses the Examiner's rejection of claims 6-8 as nonenabled. In particular, Applicant maintains that the Examiner's citation of Verma, and similar references, is not legally sufficient to establish nonenablement because (1) the instant specification clearly teaches the type of successful gene delivery Verma states is desirable; and (2) Verma only states a problem relating to *prior* gene delivery approaches, and does not teach that a peptide vector cannot solve that problem.

1. *The Examples Teach Delivery of a Gene Into Target Cells*

The instant specification amply teaches one of skill in the art how to use the claimed peptide vector to deliver and express a nucleic acid sequence to a target cell.[1] It is important to remember that claims 6 and 8 are directed to a "method of introducing and expressing a desired nucleic acid sequence comprising infecting target cells with a peptide vector". As Applicant noted in the previous Amendment, Example 4 describes the *in vivo* transfer of a peptide vector containing a green fluorescent protein (GFP)-coding sequence to different tissues in mouse. A peptide vector containing a GFP-coding sequence, constructed according to Examples 1-3 was injected into male mice. Page 11, lines 17-18. The mouse was sacrificed six days later, and mRNA was extracted from brain and muscle. Page 11, lines 19-20. The mRNA was reverse-transcribed, and PCR was performed on the resulting cDNA using GFP-specific primers. Page 12, lines 1-15. PCR showed that GFP was efficiently expressed in brain and muscle; that is, brain and muscle cells produced mRNA from the GFP sequence. Applicants therefore have demonstrated successful introduction and expression of a sequence encoding GFP, *in vivo*, using the claimed peptide vector. Moreover, because the GFP sequence used in the experiment was one designed to be expressed as a functional protein, there is every reason to believe that the mRNA is translated into functional green fluorescent protein.

Subsequent work by the inventor demonstrates that the peptide vector system works as claimed in claim 6 and 8. A similar vector was constructed and reported in Choi *et al.*, "Gene Therapy Using Non-Viral Peptide Vector in a Canine Systemic Lupus Erythematosus Model," *Veterinary Immunology and Immunopathology* 103:223-233 (2005) ("Choi"), a

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[1] The Examiner states that "Applicant refers to Examples 1-3 and lines 19-20 of page 11 . . ." Office Action, page 4. From this, it is not clear that the Examiner has fully appreciated Applicant's teaching. Applicant respectfully requests that the Examiner review the Examples, particularly Example 4.

copy of which is attached hereto. Choi describes the construction of a peptide vector constructed to contain the extracellular domain of canine CTLA-4, and the CH2-CH3 domains of canine immunoglobulin alpha constant region, between a cytomegalovirus promoter and a polyadenylation signal. *See* page 225. This peptide vector was introduced into dogs induced to develop a systematic lupus erythematosus-like disease. Dogs receiving the peptide vector showed improvements in symptomology, including improvements in alopecia, erythema, crusting, scaling and seborrhea. *See* page 229. In addition, expression of the construct delivered by the peptide vector was expressed for at least 168 days. *See* page 229. Thus, the peptide vector nucleic acid delivery system, as described in the instant application, effectively delivers, and facilitates expression of, nucleic acid sequences to target cells.

The Examiner discounts the specification's teaching by stating that "it does not overcome the problem of gene delivery to targeted cells . . . it does not solve the problem of transient expression. . . [and] it fails to show that the transferred protein [*sic*] was translated so that the desired protein would be expressed . . ." Office Action, page 4. Applicant addresses each of these in turn.

First, Applicant respectfully suggests that the Examiner is incorrect in stating that the peptide vector does not overcome the problem of gene delivery to targeted cells. As explained in Example 4 of the specification, a peptide vector was used to deliver GFP cDNA into brain and muscle cells. This cDNA was detectable in these brain and muscle tissues *six days* after intravenous injection of the vector, indicating that delivery to these tissues had, indeed, taken place. The peptide vector therefore *does* overcome the problem of gene delivery to a targeted cell.

Second, there is no requirement for *enablement* purposes that the claimed peptide vector "solve the problem of transient expression." Office Action, page 4. "Overcoming transient expression" is not a requirement for enablement stated in the patent statutes, the Code of Federal Regulations or the Manual of Patent Examining Procedure. In fact, the sole basis for this objection appears to be a statement in Verma, cited by the Examiner, that "transient expression of the transgene is a conceptual hurdle that needs to be addressed." Verma, page 239, third column. Verma, however, does not state a requirement for *enablement*, but a *scientific challenge*. Nothing in Verma - and nothing in the patent laws - states that a vector delivering a gene that is transiently expressed would be without value for treating an individual. Stable expression may be more desirable for certain applications,

while for other applications, transient expression may be more desirable. This objection is not, therefore, a legally sufficient basis for a nonenablement rejection.

Moreover, the Examiner provides no indication that the claimed peptide vector dose *not* provide stable expression of a transferred gene. Indeed, the fact that GFP mRNA was detectable six days after the peptide vector's administration argues that expression in this system *is* stable. *See also* Choi, above.

Finally, the Examiner's contention that the Example does not "show that the transferred protein was translated so that the desired protein would be expressed at sufficiently [*sic*] levels to produce a desired function in the target cells" is without basis; there is no reason to believe that the GFP mRNA produced in the experiment did not produce active GFP. There is also no reason to believe that mRNA from other transferred polynucleotide sequences, where the polynucleotides sequences were designed to encode functional proteins, would not encode functional proteins.

Therefore, the specification shows delivery by the peptide vector of a nucleic acid sequence to target cells *in vivo*, followed by production of mRNA and protein. This is confirmed by the work of Choi *et al.* Claim 6, as amended, and claim 8 are, therefore, enabled by the specification.

2. *Verma Is Not The Standard For Enablement*

Second, Verma, and the remaining articles cited by the Examiner, do not teach a legal standard by which enablement is to be judged. The Examiner does not argue that the invention as claimed in claims 6-8 would require undue experimentation. Rather, the Examiner states that Verma (*Nature* 389:239-242) "discusses a substantial hurdle [delivery of nucleic acid into the cell] that must be overcome to *enable* gene therapy methods and discloses that this hurdle is an obstacle to non-viral delivery methods such as the one claimed by Applicant."[2] Office action, page 3 (emphasis added). Thus, the Examiner cites Verma for its teaching that previous gene delivery methods are problematic because they do not adequately deliver nucleic acid into the cell. The Examiner appears to assume that, in order to be enabling, the current specification must *solve* all of the gene delivery problems of the

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[2] In fact, as Applicant has pointed out, Verma devotes the bulk of the article - three out of four pages - to problems inherent in the use of *viral vectors*, and mentions non-viral delivery methods only in passing.

prior art as explained in Verma and other references cited by the Examiner. This is clearly not the standard for nonenablement. Neither Verma, nor the other references cited by the Examiner, address in any way the peptide vector, the type of vector that Applicant currently claims. Verma is particularly irrelevant because Applicant *has* demonstrated delivery of a gene to target cells *in vivo*. Verma, and the remaining references cited by the Examiner, simply cannot inform one of skill in the art as to whether the currently-claimed peptide vector is enabled or not. The best source of information on the peptide vector is, instead, the instant specification.

Thus, (1) the specification enables claims 6 and 8; and (2) Verma, and similar references, do not constitute a legal standard for enablement mandating rejection of claims 6 and 8. Applicant therefore respectfully requests that the Examiner withdraw the rejection of claim 6 and 8 on this basis.

The Rejection Under 35 U.S.C. § 112, First Paragraph,
For Lack of Written Description, Should Be Withdrawn

The Examiner has rejected claims 1 and 6 under 35 U.S.C. § 112, first paragraph, for lack of written description support. Applicant has amended claims 1 and 6 to include the limitations of claims 2 and 7, respectively. Claims 2 and 7 have been canceled. Applicant thanks the Examiner for noting that claims 2 and 3 would be allowable if rewritten in independent form; the amendment of claim 1 effectively accomplishes this rewriting. Therefore, claims 1 and 3 should now be allowable. Likewise, Applicant maintains that the amendment of claim 6 to include the limitations of claim 7 should obviate the written description rejection with respect to claim 6. Applicant therefore respectfully requests that the Examiner withdraw the rejection of claim 1 and 6 on this basis.

CONCLUSION

Applicant respectfully requests entry of the foregoing remarks into the file of the above-identified application. Applicant believes that all the pending claims are in condition for allowance. Withdrawal of the Examiner's rejections and allowance of the application are respectfully requested.

Respectfully submitted,

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